FACULTY OF BIOSCIENCE ENGINEERING

DEPARTMENT OF ANIMAL SCIENCES AND AQUATIC ECOLOGY
Research Unit: GhEnToxLab (Environmental Toxicology)
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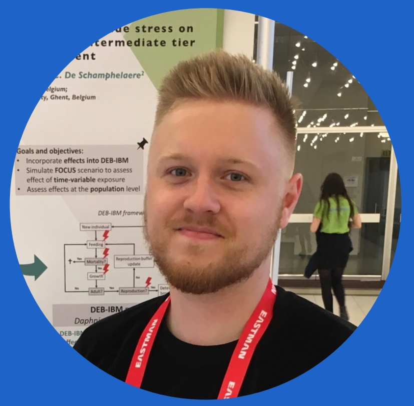
UNEXPECTED RECOVERY AND NON-EFFECTS PREDICTED WITH A MIXTURE TOXICITY IMPLEMENTATION IN A POPULATION MODEL

Karel Vlaeminck[1,2], Karel Viaene[2], Patrick Van Sprang[2] and Karel De Schamphelaere[1]

[1]GhEnToxLab, Ghent University, Coupure Links 653 – Building F 2nd floor, 9000 Ghent, Belgium

[2]Arche Consulting, Liefkensstraat 35D, 9032 (Wondelgem) Ghent, Belgium



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AGENTSCHAP INNOVEREN & ONDERNEMEN

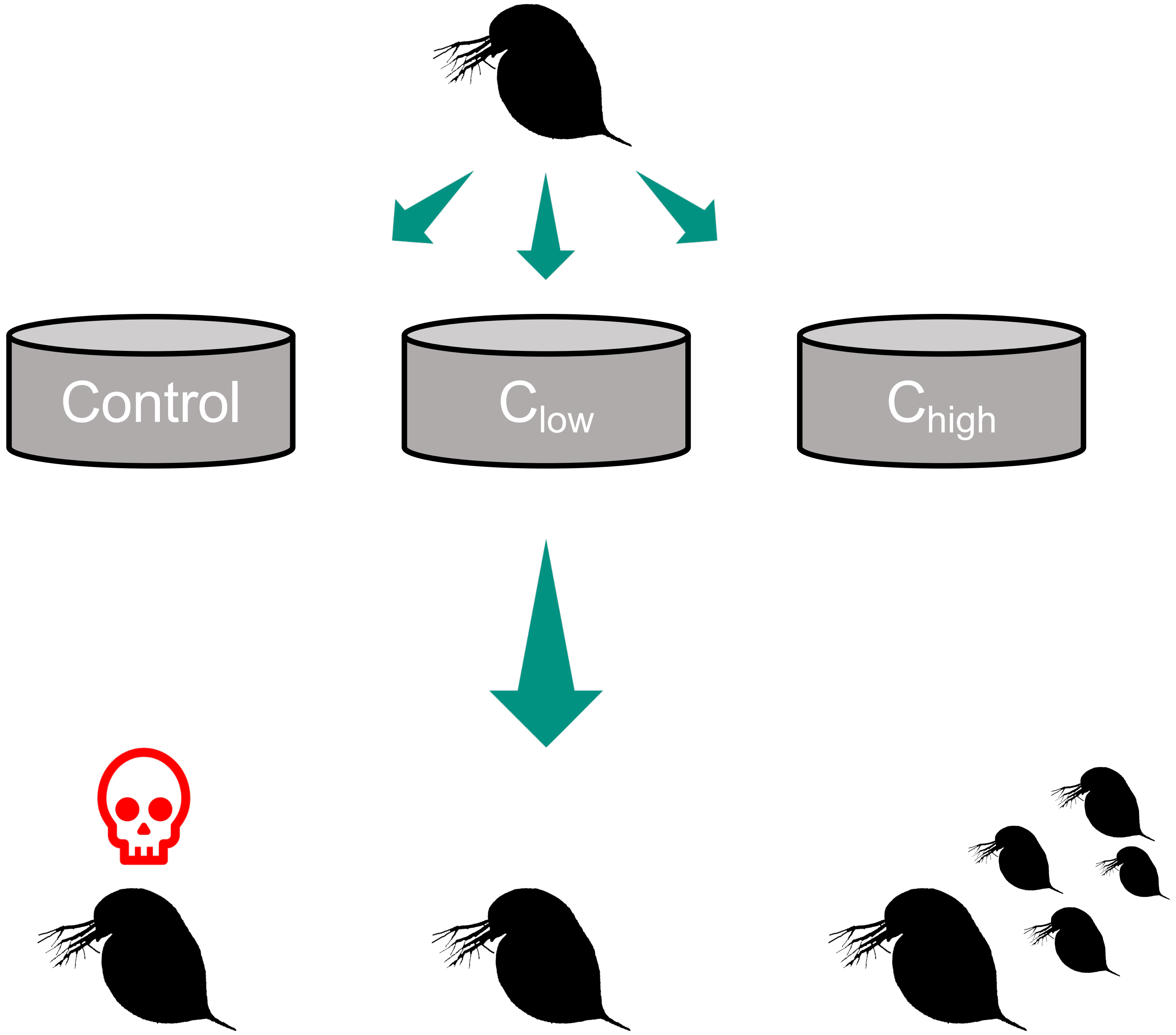
Vlaanderen is ondernemen

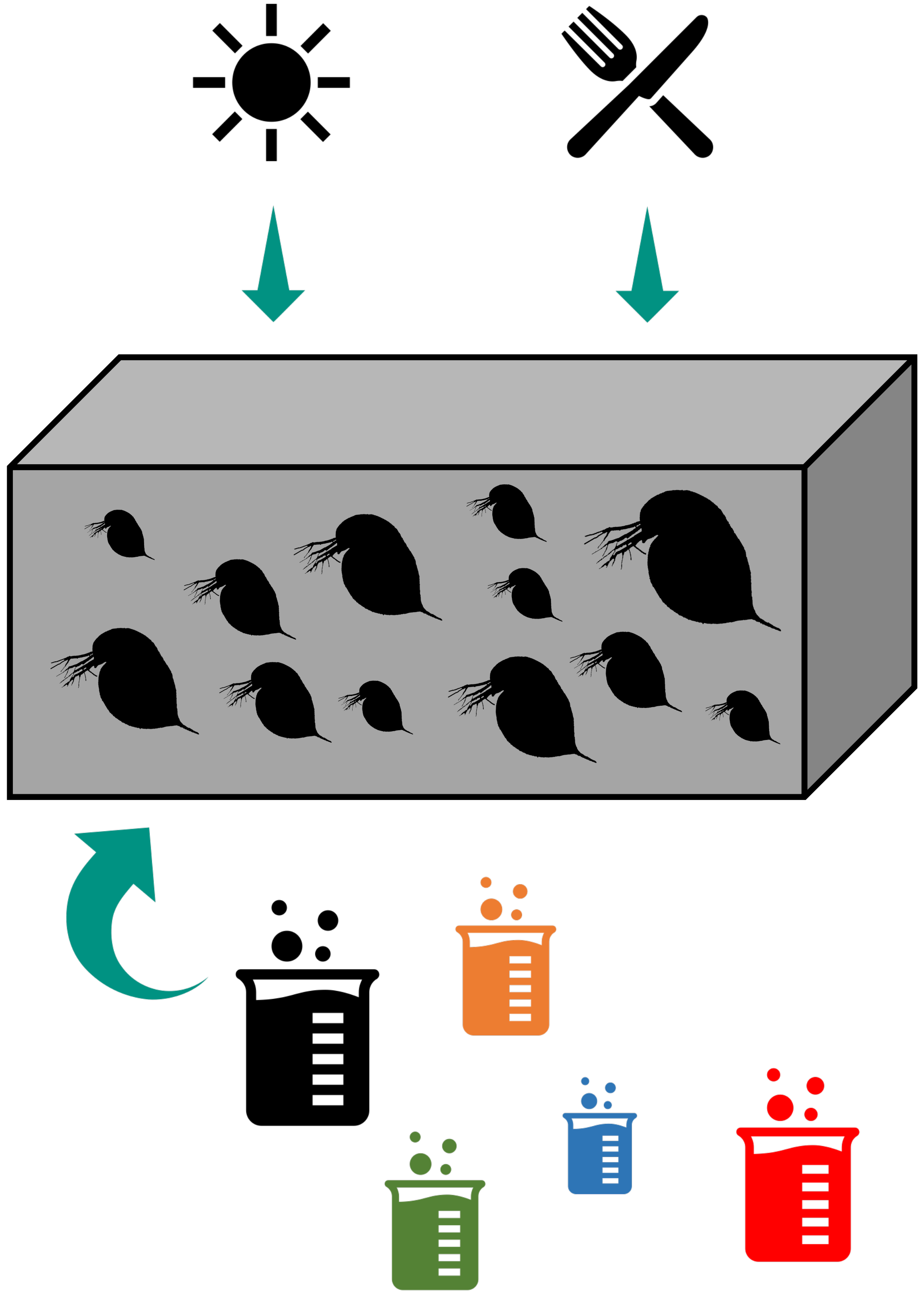
Cu European Copper Institute Copper Alliance

International Zinc Association

Zinc...essential for modern

RISK ASSESSMENT VS THE ENVIRONMENT





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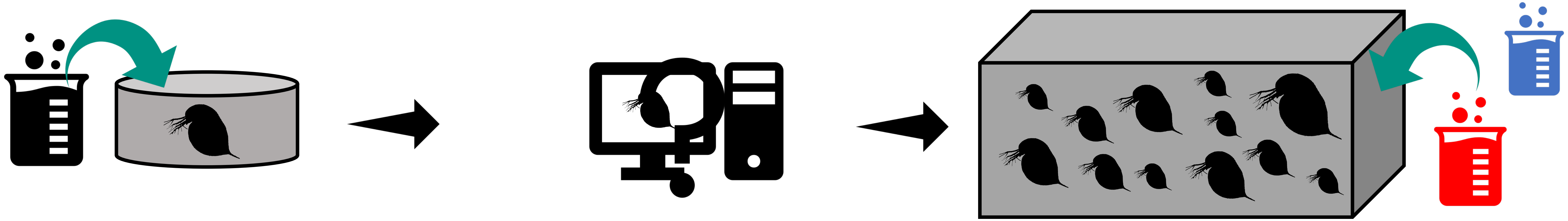
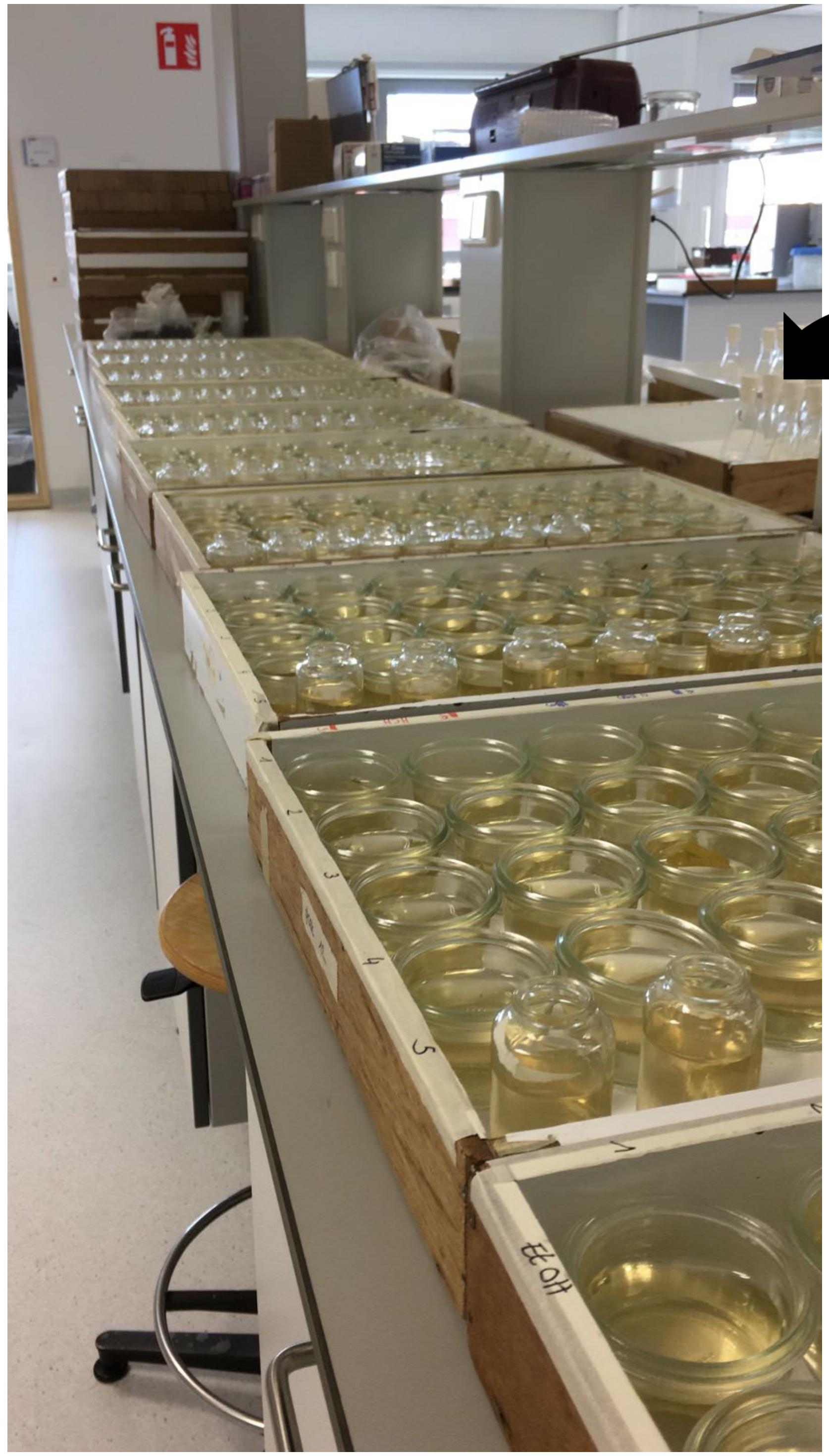
APPARENT MISMATCH



Standardized tests	Reality
Individuals	Populations within communities in the ecosystem
Single compounds	Mixtures of compounds
Constant concentrations	Variable exposure concentrations

So far, applications of <u>mechanistic models</u> for <u>mixture toxicity</u> in a <u>population context</u> are, to our knowledge, limiting

EXPERIMENTAL WORK: DATA GENERATION

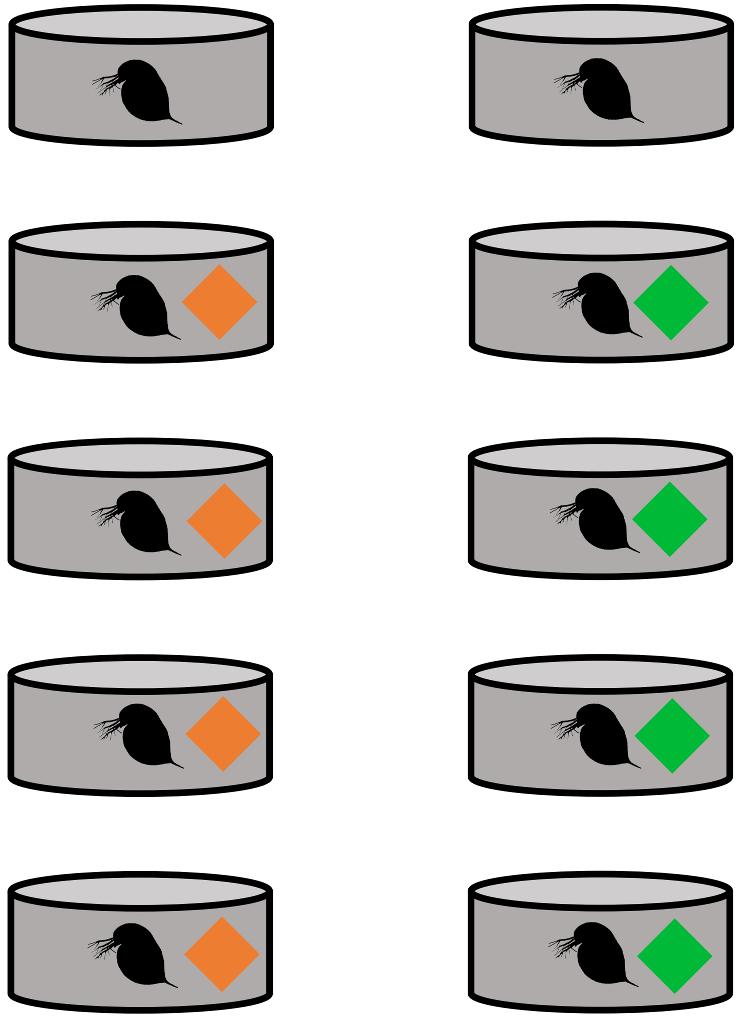


Generate data for model <u>calibration</u>

Assess individual-level effects of individual substances to *Daphnia magna:*

- Growth
- Reproduction
- Survival over time

Standard 21-day chronic reproduction test at the individual level

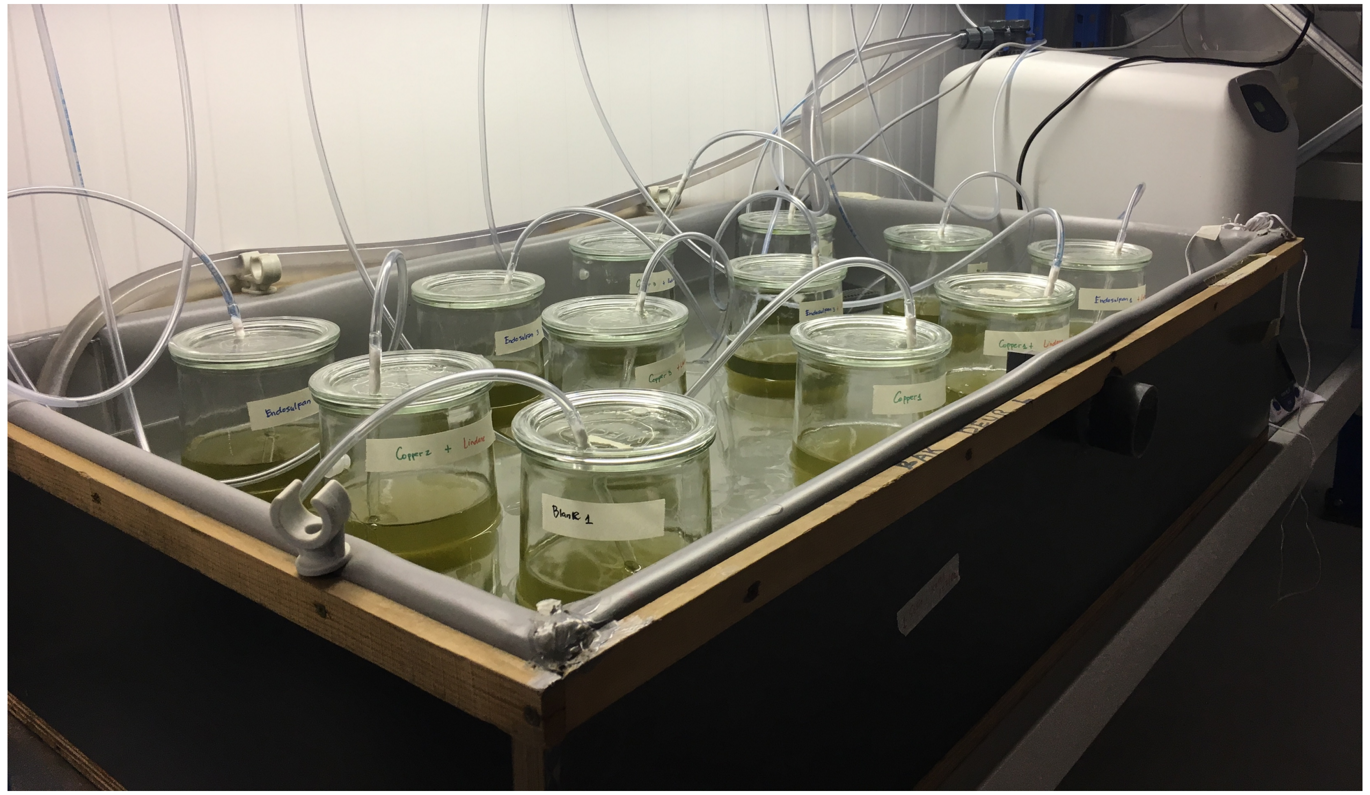


5 concentrations per compound + control
All in replicates of 10

EXPERIMENTAL WORK: DATA GENERATION

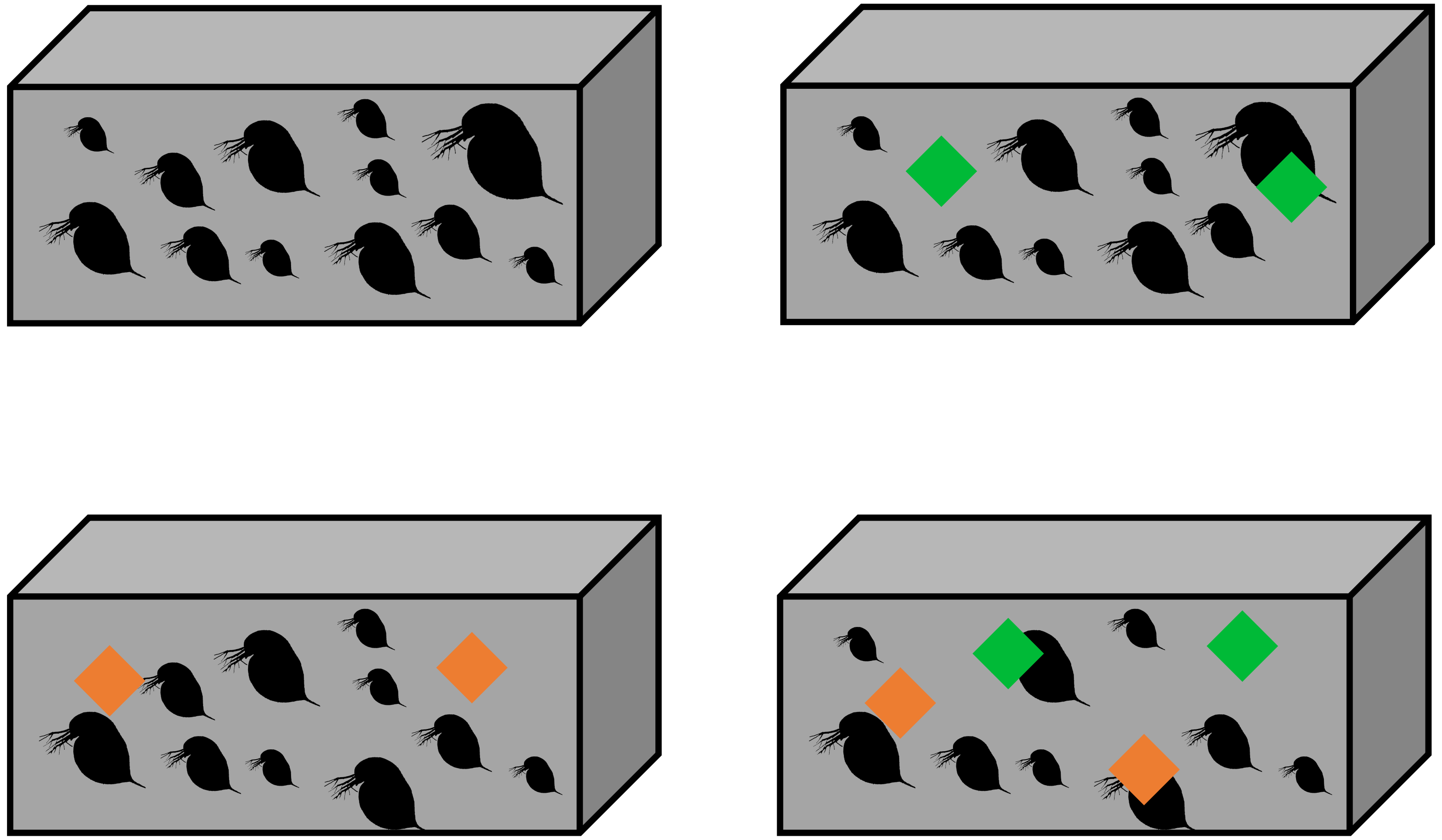
Generate data for model <u>validation</u>

Population-level effects of chemical mixtures to *D. magna* populations



Assess **population density** over time

"Standard" population experiment with mixtures with a 75-day exposure duration



2 Zn and 2 Cu conc + their 4 mixtures + control
All in replicates of 4 (= 36 aquaria in total)

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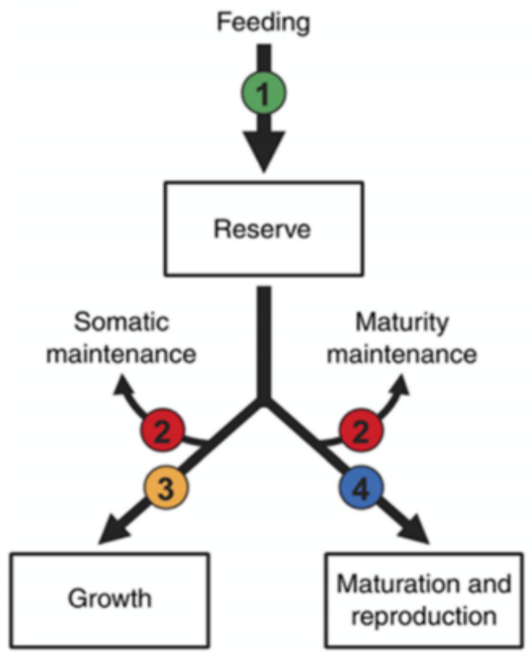
MODEL VALIDATION AND SCENARIO ANALYSIS

Develop <u>mechanistic population model</u>: ***TKTD + DEB + IBM = population effects***

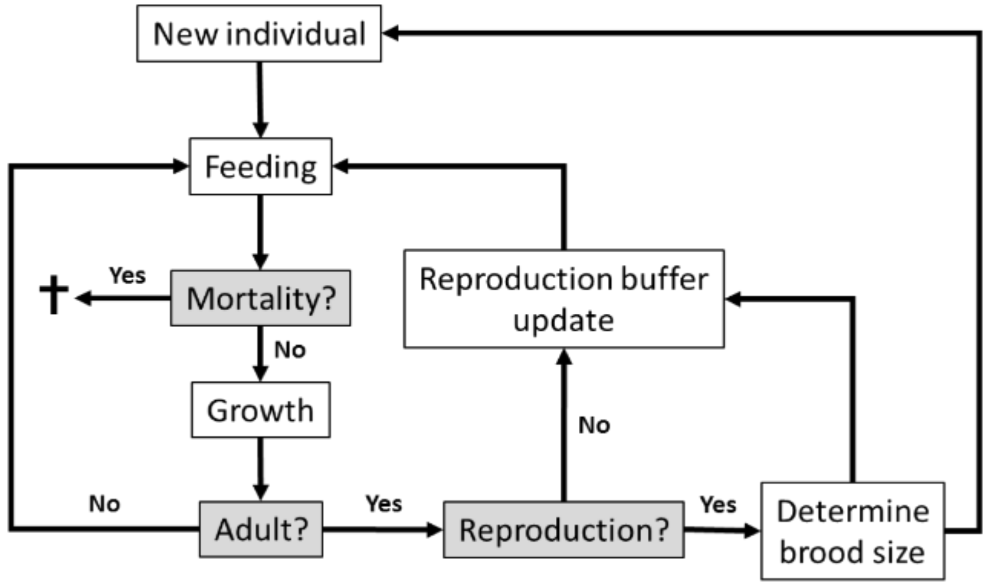
Toxicokinetics
Toxicodynamics

Chemical A
Chemical B
Chemical C
…

DEB model



IBM framework



Population endpoints over time

Population reproduction
Carrying capacity
Age structure
Recovery over time
…

DEB image: from Martin et al. (2013)
IBM image: from Viaene (2016)

Toxicokinetics-toxicodynamics (TKTD) to describe lethal and sub-lethal effects of each chemical

Dynamic energy budget (DEB) model to describe organism (feeding, growth, reproduction)

Individual-based model (IBM) framework to predict population dynamics over time

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MIXTURE TOXICITY IN MECHANISTIC MODELS

Two reference models for <u>mixture toxicity</u> effects:

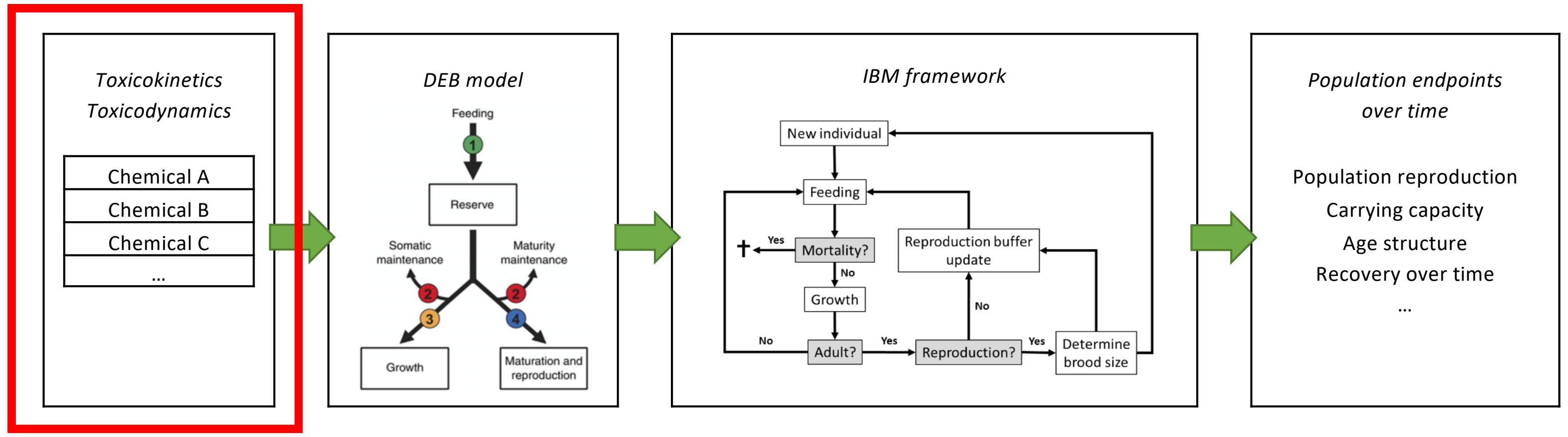
General (statistical) mixture toxicity models

Equations from Nys et al. (2018)

Independent action (IA)	Concentration addition (CA)
$y_{mix} = \prod_{i=1}^{n} y_i$	$\sum_{i=1}^{n} \frac{C_i}{ECx_i} = 1$

Mechanistic models, e.g. DEBtox (Jager et al. 2010) and GUTS (Jager and Ashauer 2018)

Independent action (IA) ✓	Damage addition (DA) ✗



DEB: ORGANISM-LEVEL

IA is calculated at the level of the **Physiological Mode of Action (PMoA)**

$$C_w \xrightarrow{\text{TKTD}} D_w \xrightarrow{\text{Effect mechanism}} \text{PMoA}$$

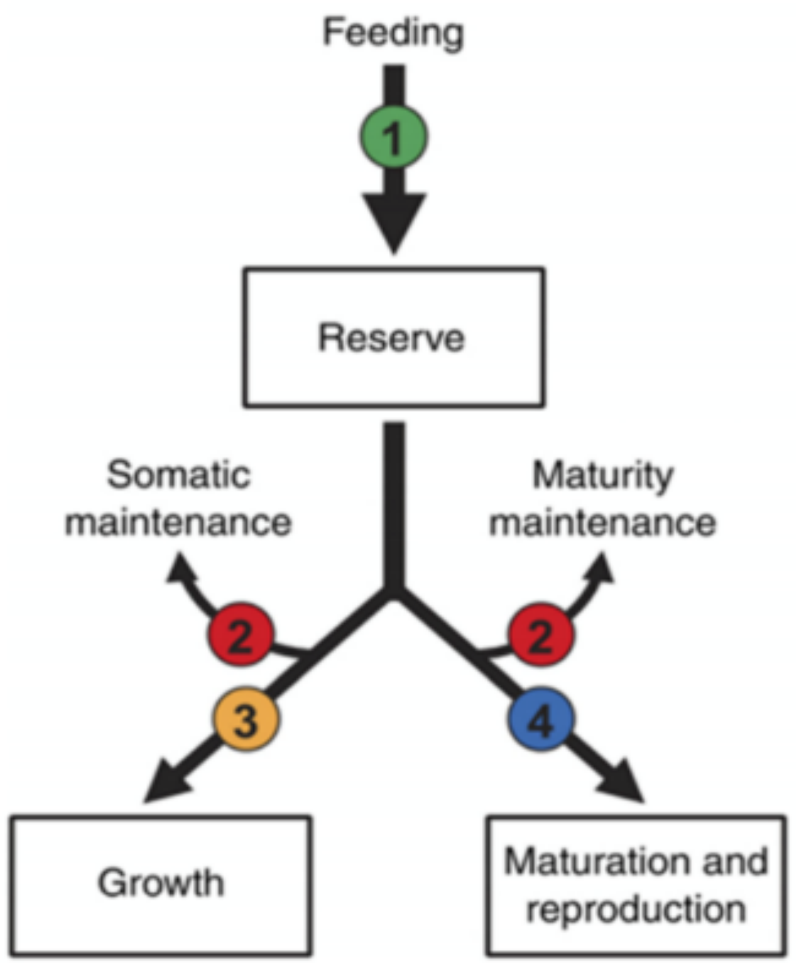
IA assumes the **effect is independent:**

- Different PMoA
- Effect is multiplied when same PMoA

Reproduction efficiency

$$\kappa_{R,s} = \frac{\kappa_R}{(1+s_1)*(1+s_2)}$$

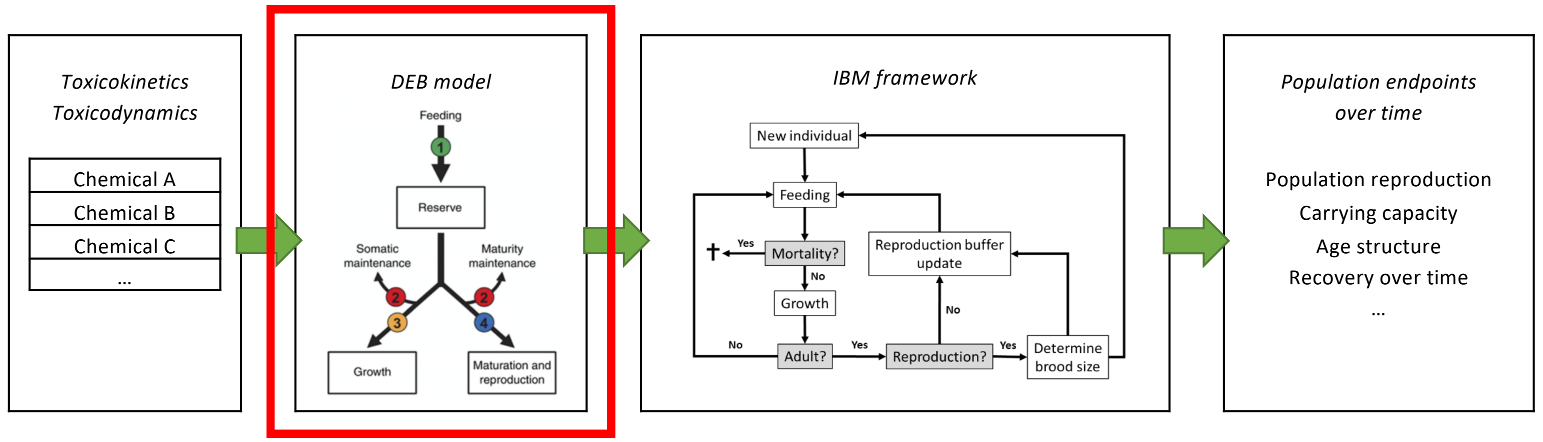
Stress on PMoA due to compound 1 and 2



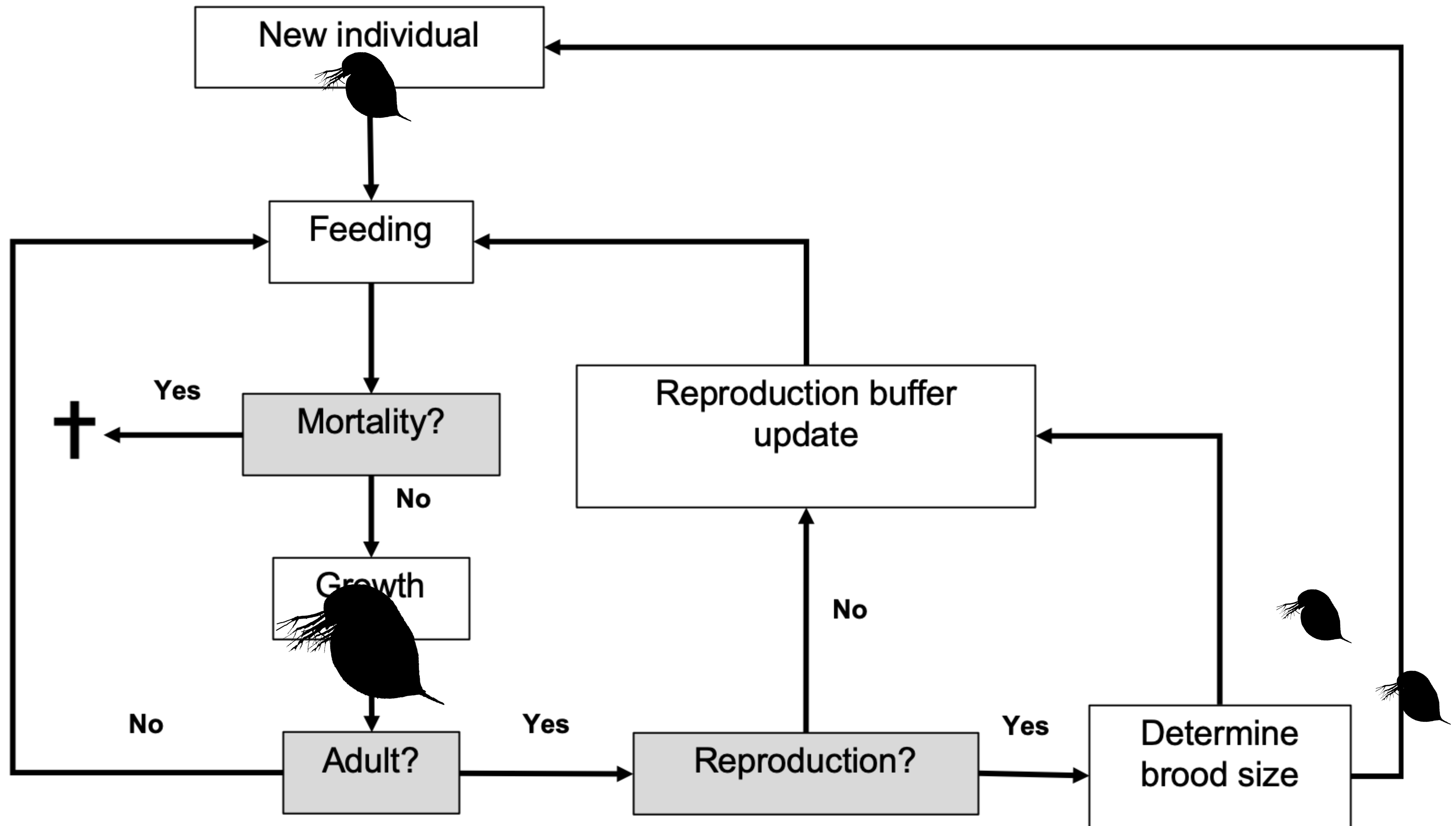
DEB image: from Martin et al. (2013)

Effect mechanism:

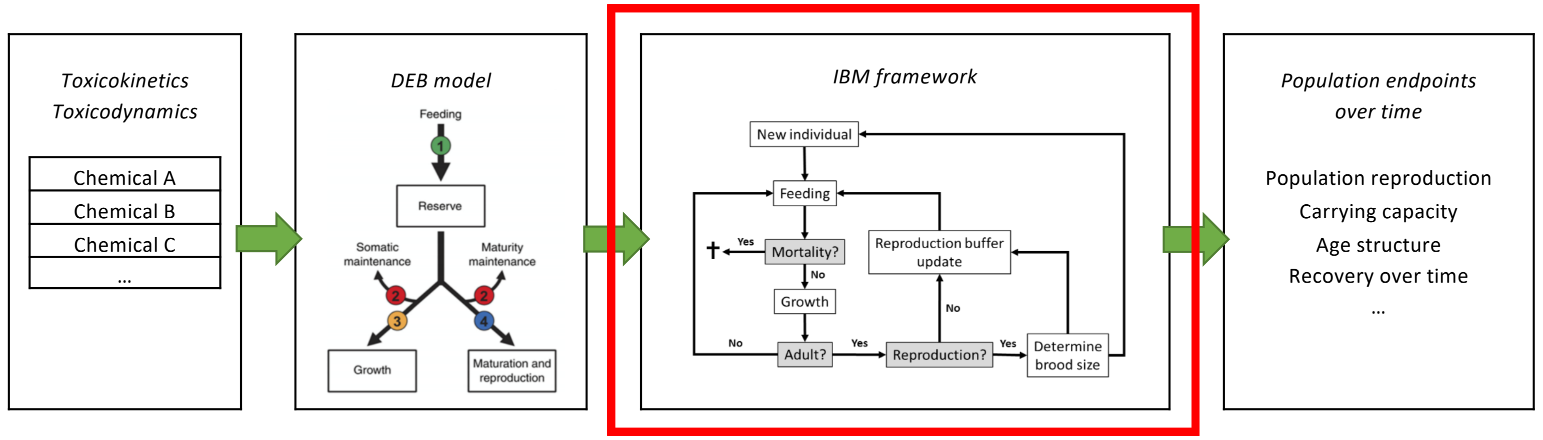
- **DEBtox** (Jager 2017) for sub-lethal effects
- General Unified Threshold theory for Survival (**GUTS**) for lethal effects (Jager and Ashauer 2018)



IBM: POPULATION DYNAMICS



IBM image: from Viaene (2016)



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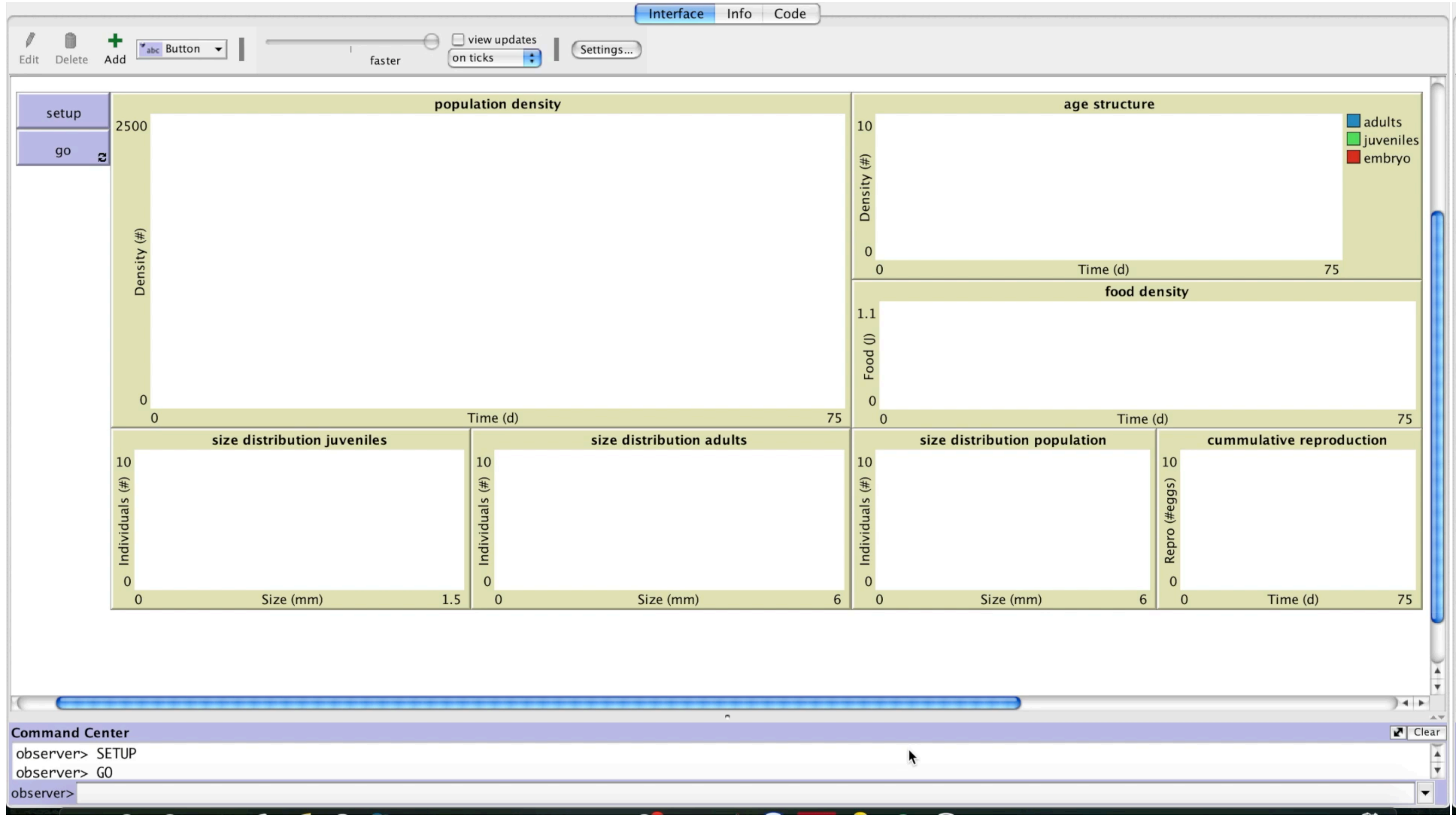
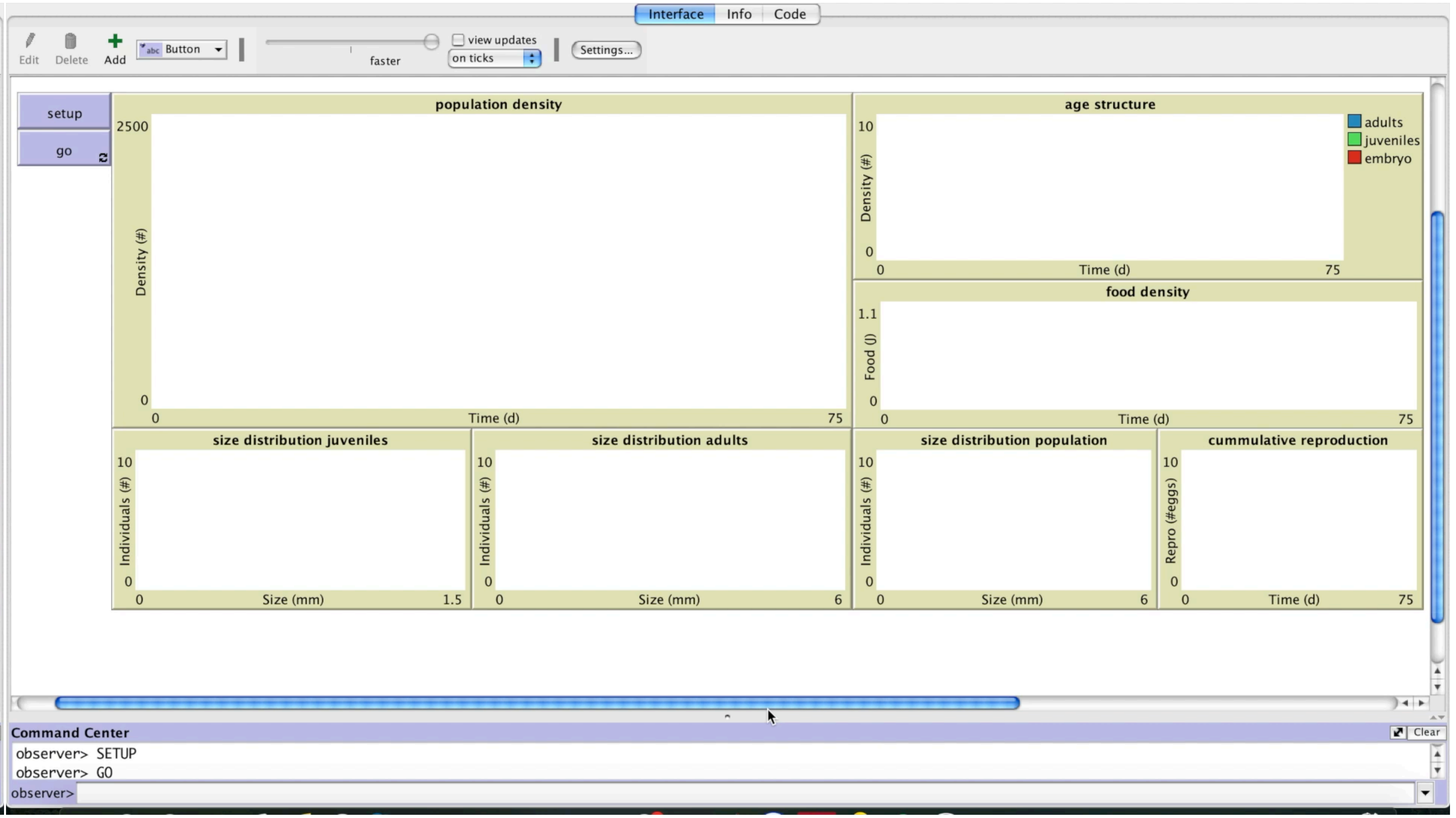
IBM: POPULATION DYNAMICS

Control simulation (no stressors)



Exposed simulation (50 μg Cu/L)



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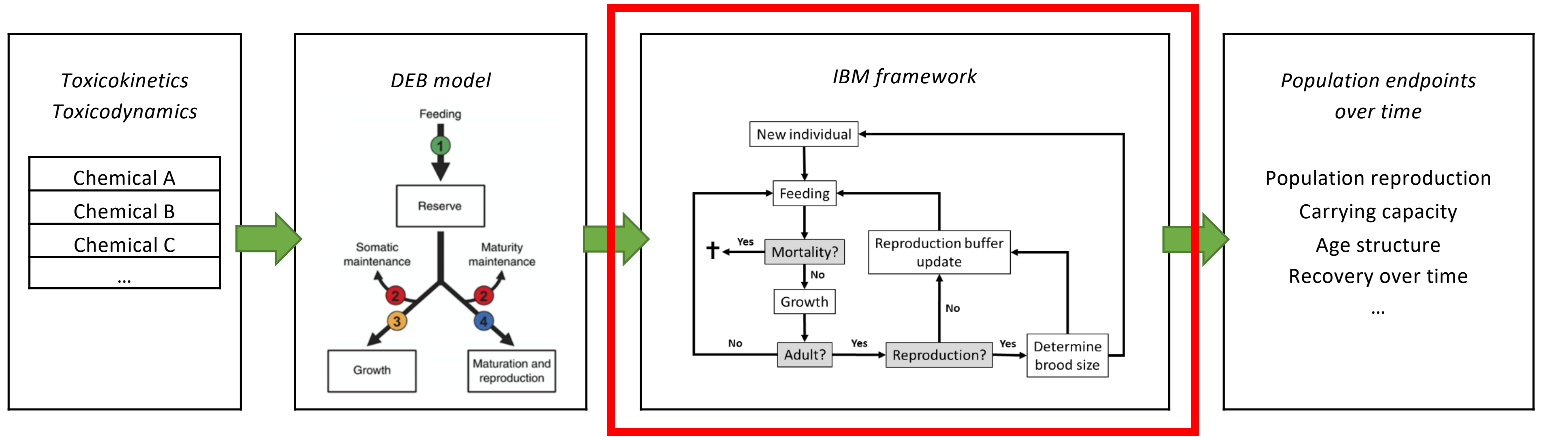
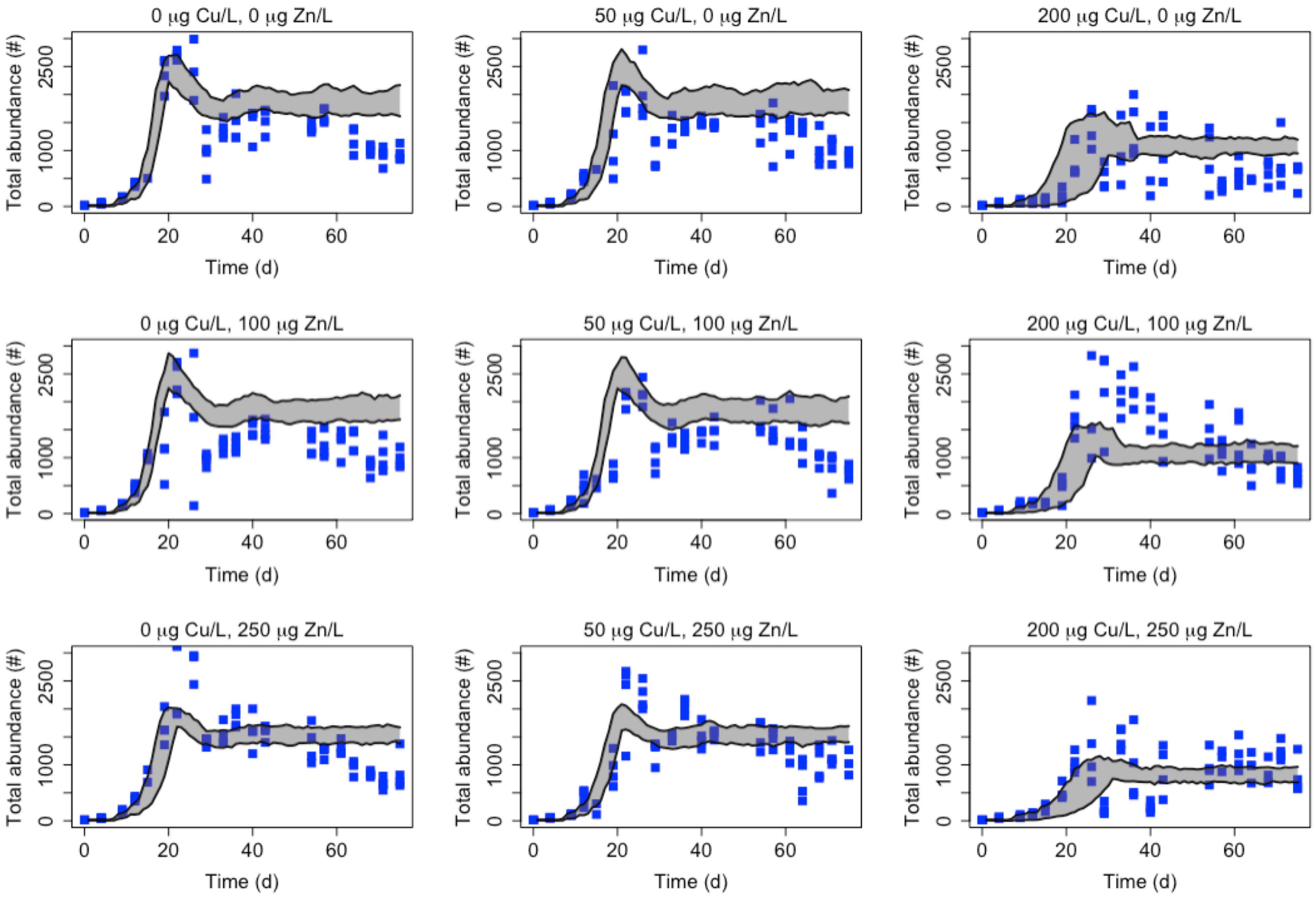
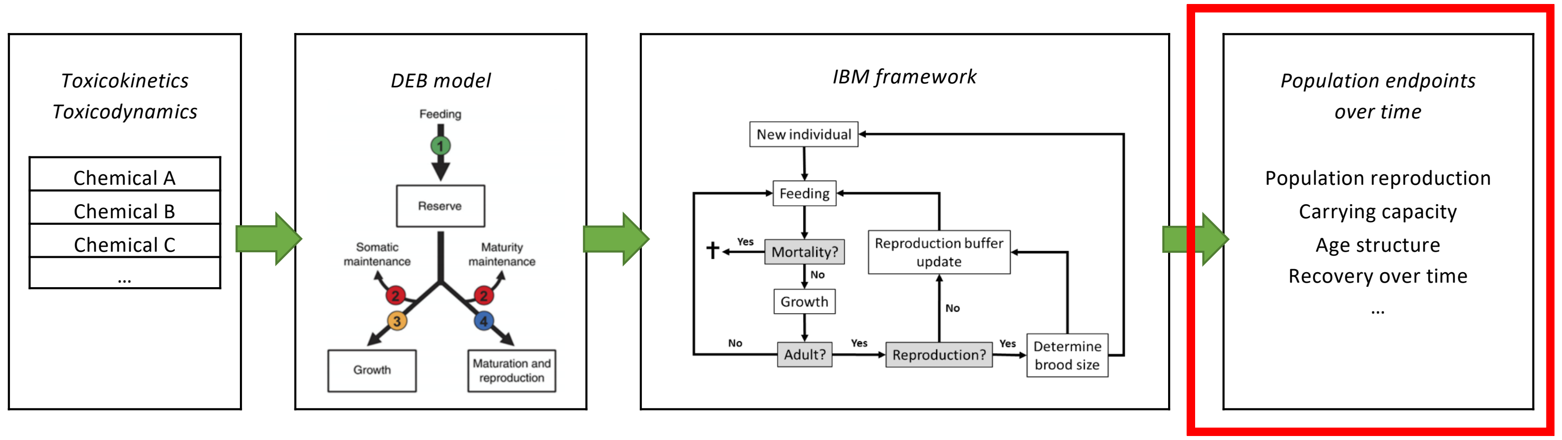


RESULTS: INDEPENDENT ACTION

Cu
Zn





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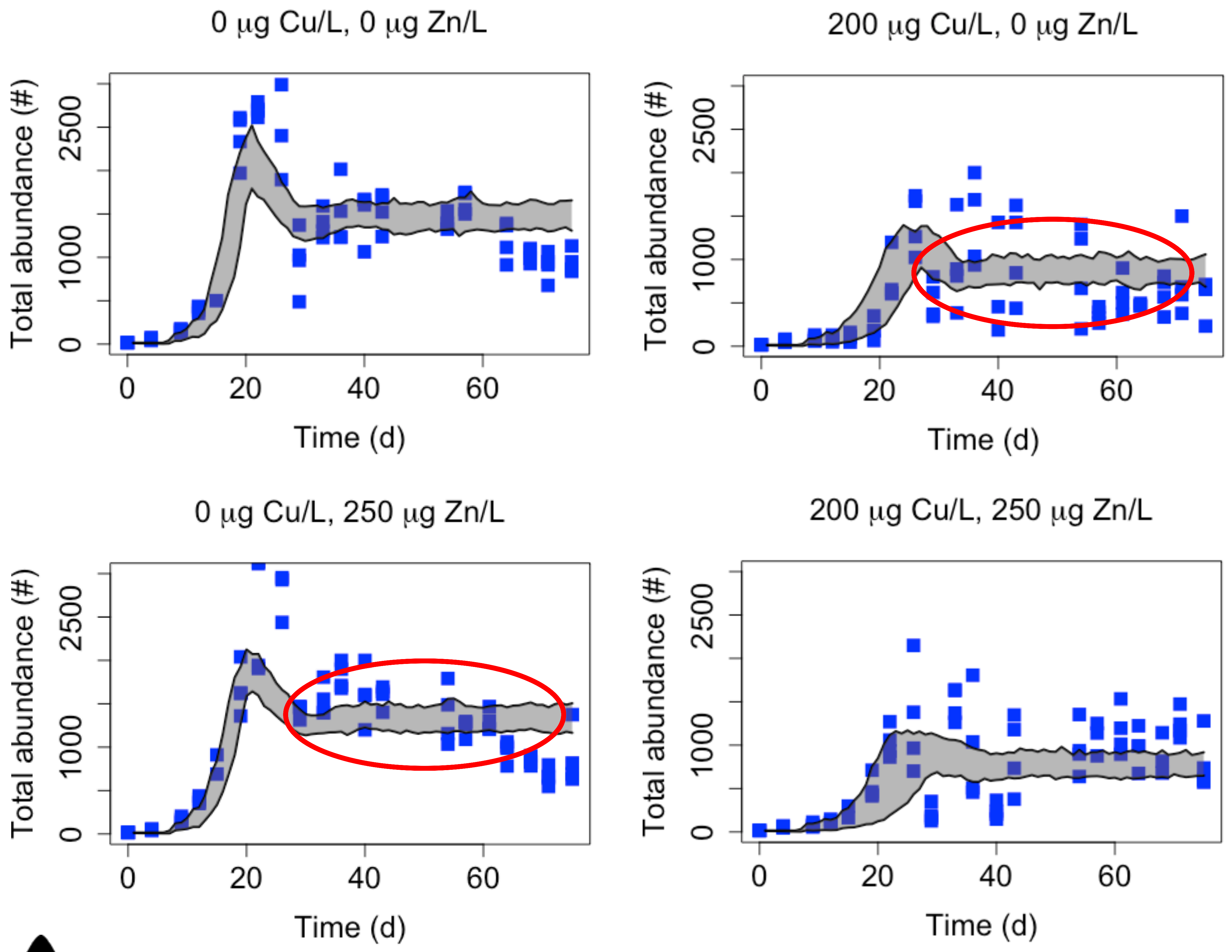
RESULTS: INDEPENDENT ACTION

Cu

Zn

General population dynamics are captured well by the model (growth and equilibrium phase)

Apparent absence of significant Zn effects at the population level was correctly predicted by the model



Cu significantly reduced population growth rate and mean population density at equilibrium

Model captures general trend in population dynamics observed, and effects

Mixture toxicity effects are predicted correctly

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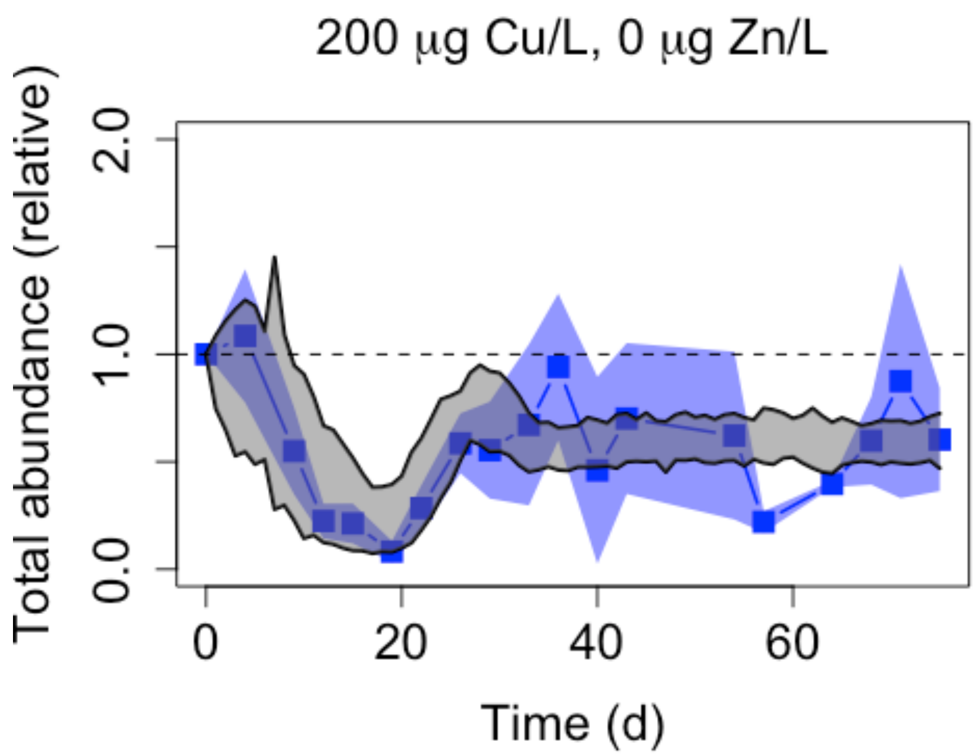
RELATIVE EFFECTS

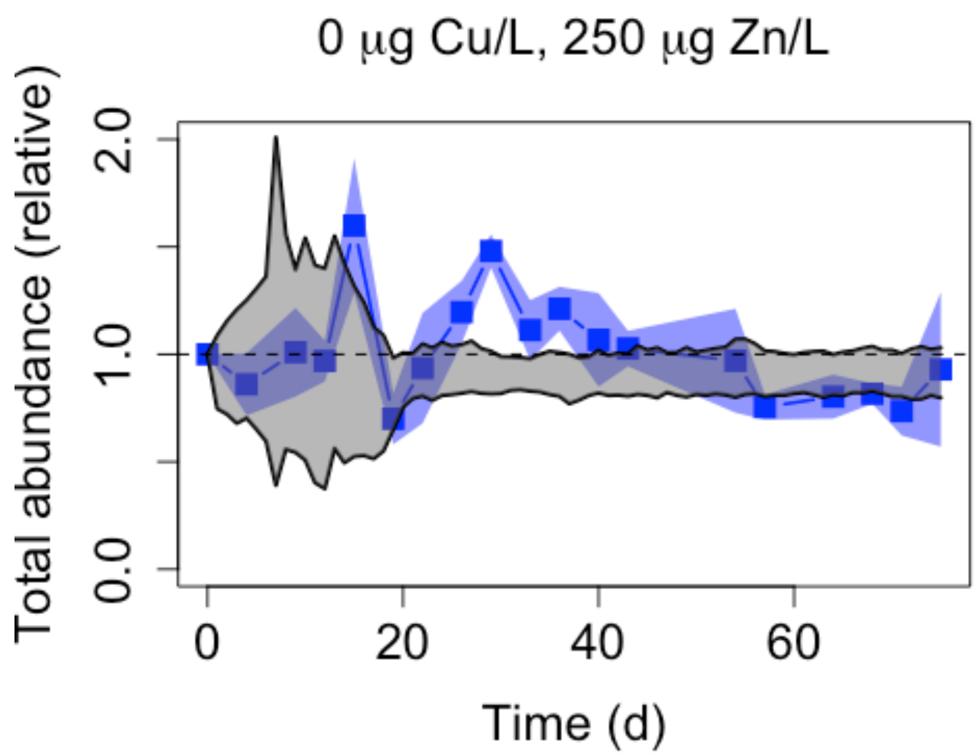
Relative effects:
- Data is divided by the control data
- Predictions are divided by the control simulations

Cu



Initially a large effect of Cu is observed and predicted
Unexpected recovery of effects over time is observed and predicted

Absence of Zn effects at the population level although we tested **relevant concentrations**: 88.7 and 182.5 µg Zn/L



Zn

Individual-level LCx values:
21-day LC10 and LC50 of 89 and 204 µg Zn/L

Similar patterns observed with Ni (Pereira et al. 2019)

How to explain these trends?

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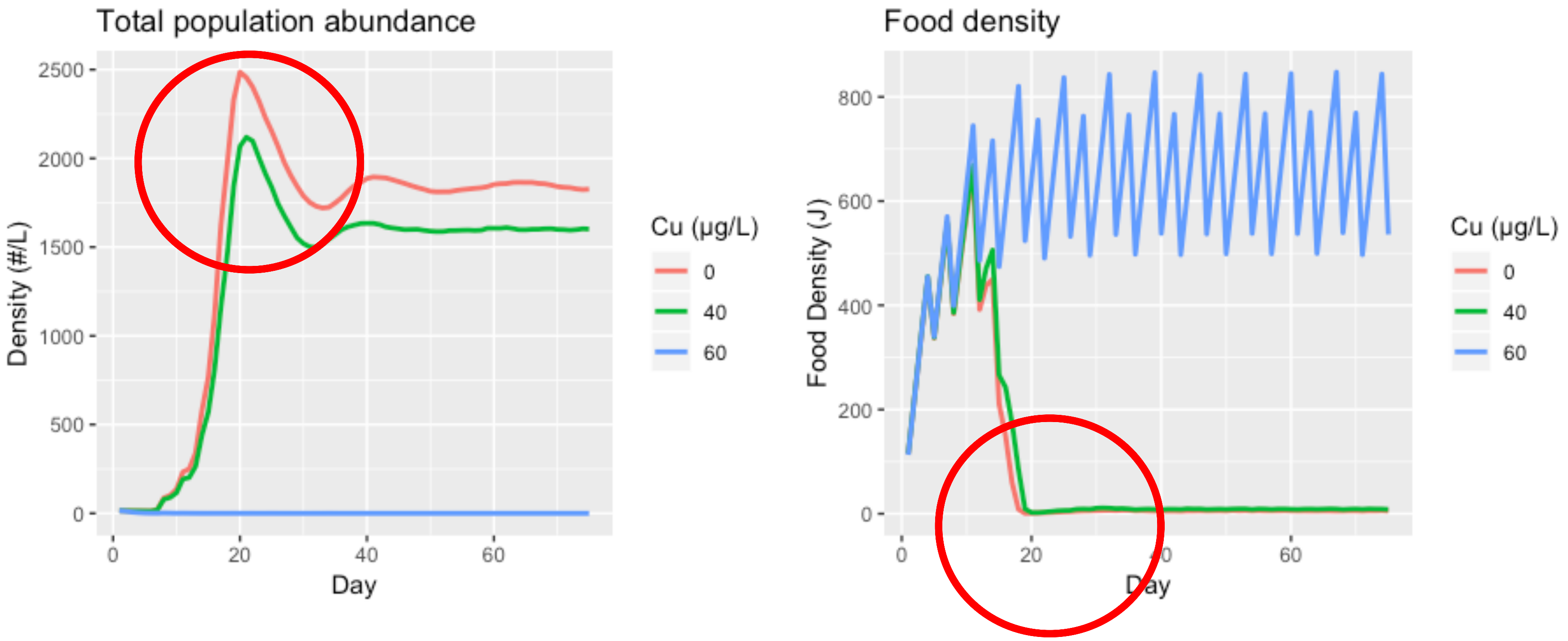
MODEL AS TOOL TO EXPLAIN TRENDS

Cu

Zn

Use the model to explain the observed trends

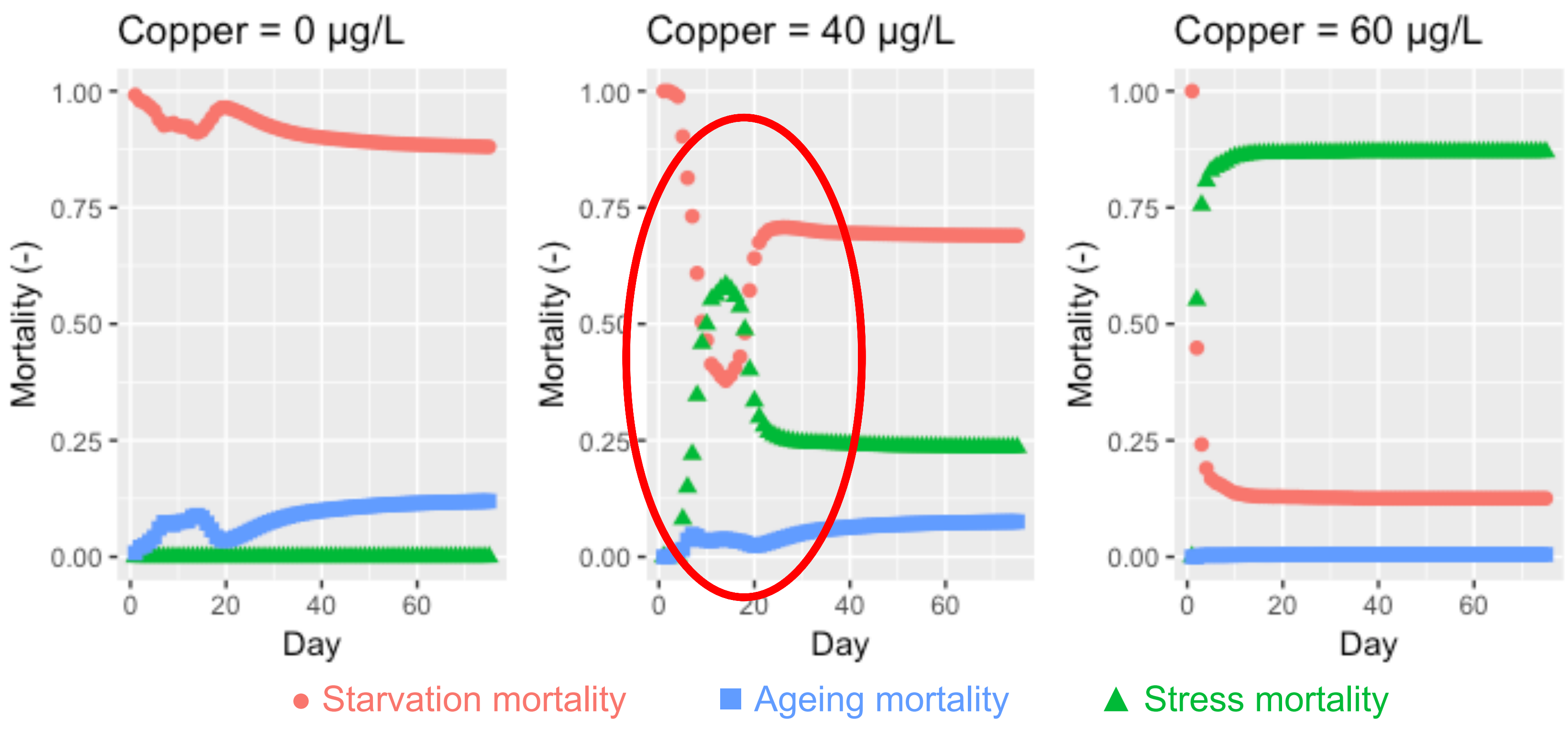
Track state variables of individuals and the environment in the IBM simulation



Peak density is reached when food becomes limiting
Food limitation will lead to starvation

Track mortality causes in the simulation

Switch from dominant starvation mortality to stress mortality in growth phase



Switch back **when food becomes limiting** explains the recovery

Compensation due to decreased starvation mortality at the population

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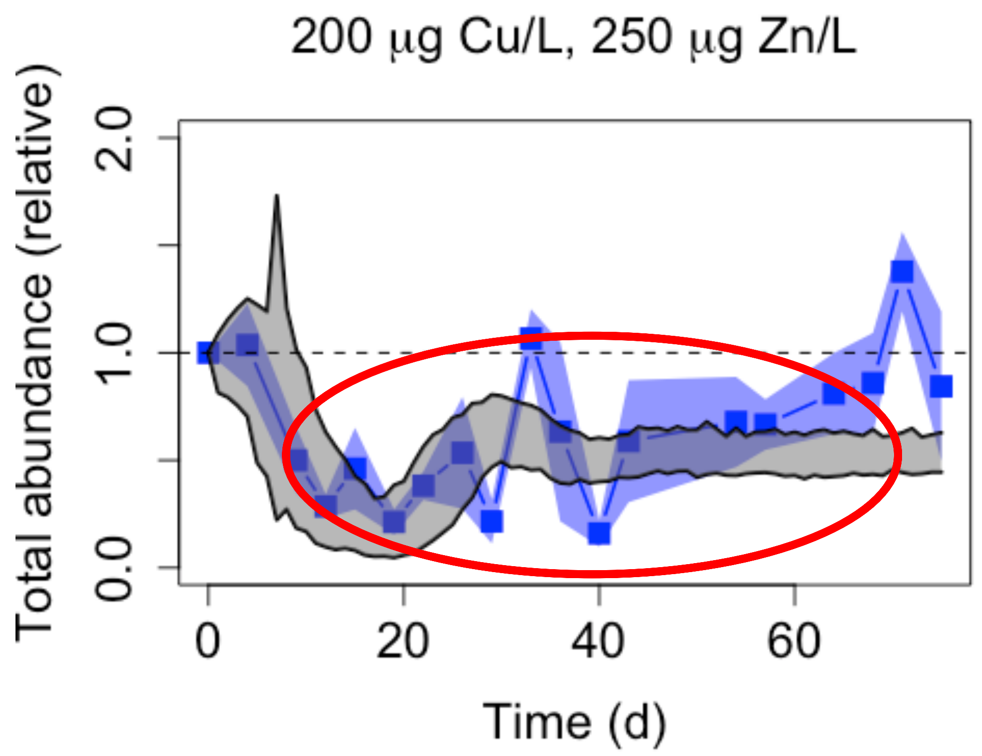
MIXTURE TOXICITY EMERGES

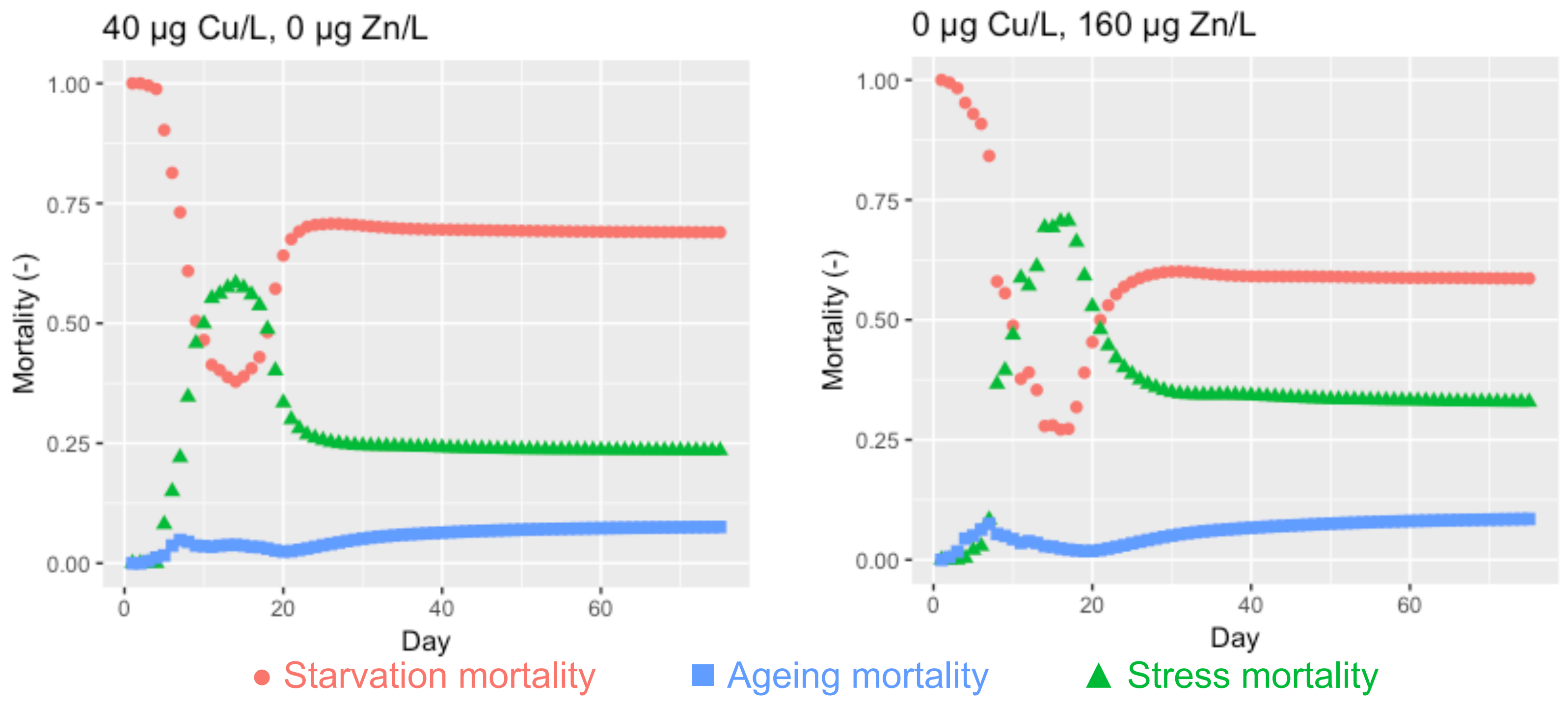
Mixture toxicity effects emerge from the IA model implementation

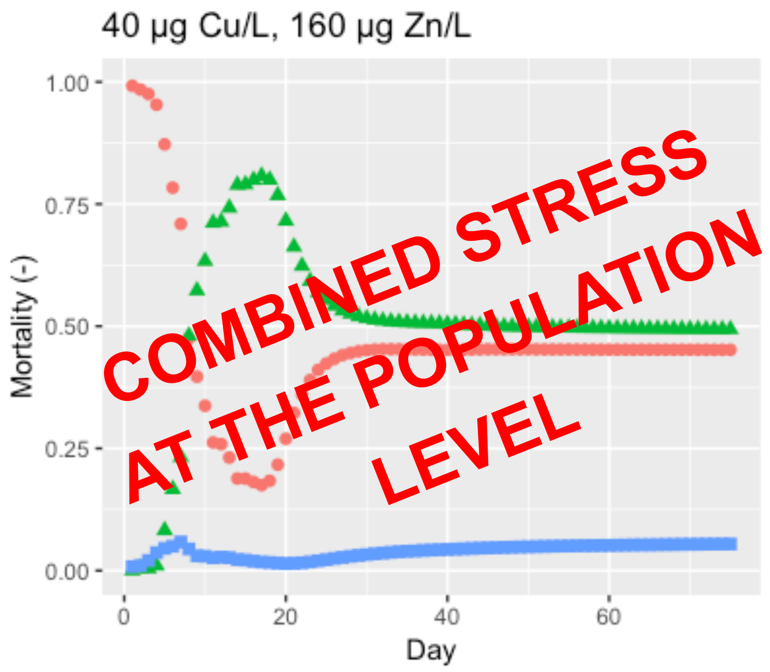


Significant delay in growth and decrease in equilibrium population density

Recovery over time when looking at relative effects

Go deeper in the model to **investigate mixture toxicity effects**





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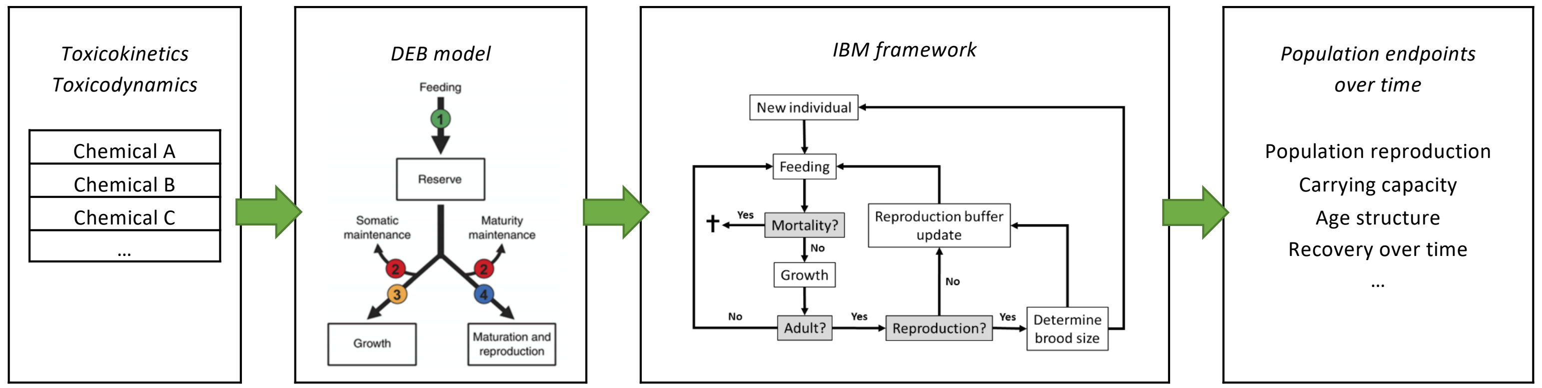
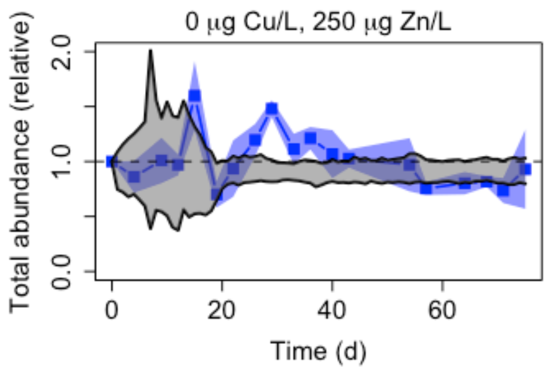
TAKE-HOME MESSAGE

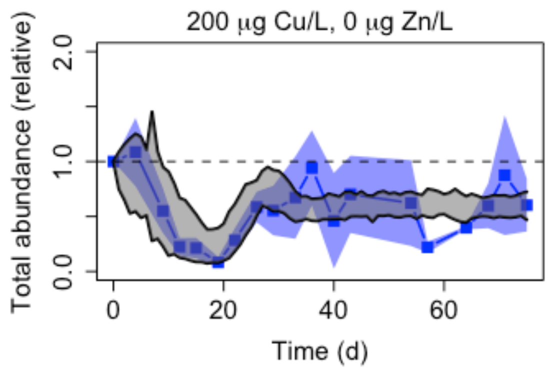
1. Realistic extrapolation with DEB-IBM



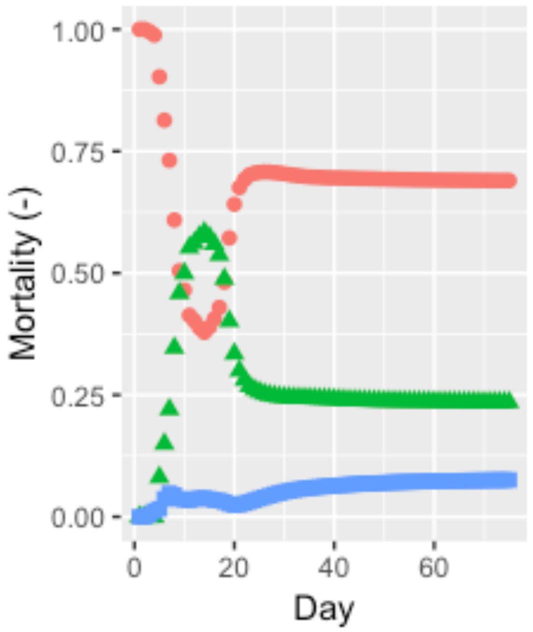
2. Non-effects confirmed



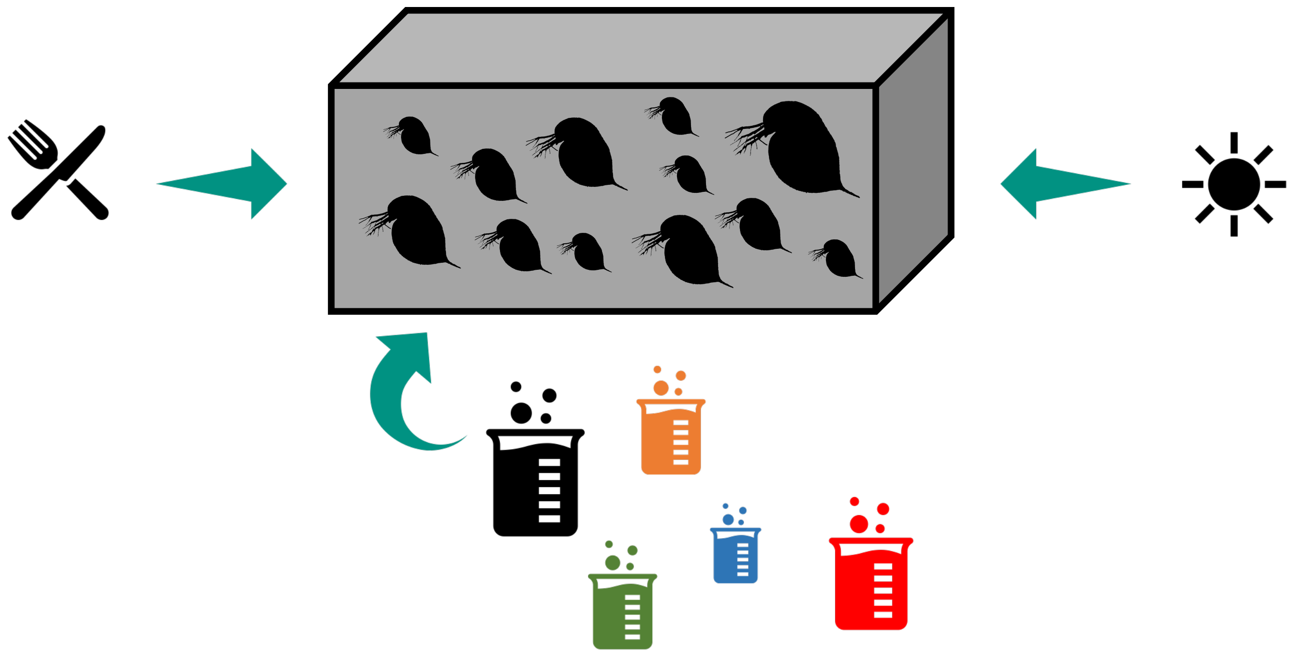
3. Unexpected recovery



4. Predict mixture toxicity at the population level



5. More realism and ecological relevance



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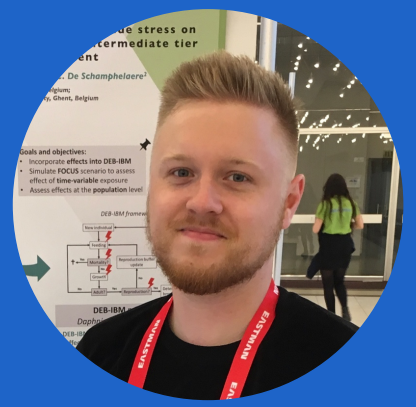

Join me in the Q&A: Monday (May 4th), 13h00 – 13h45

Contact me: Karel.Vlaeminck@UGent.be

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And visit our other (modelling) platforms and posters:

3.20.1	**Karel Viaene**	Ecorelevance: Population modelling for metal risk assessment
3.20.2	**Sharon Janssen**	Integrating bio-availability of metals in fish population models
2.05.5	**Simon Hansul**	Predictive Modelling of Metal Mixture Toxicity to Daphnia magna Populations
4.07P.11	**Kristi Weighman**	Developing a DEB-IBM to predict population level effects of Ni on the great pond snail, *Lymnaea stagnalis*
4.07P.14	**Sharon Janssen**	Multiple individual-level toxicity effects on an *Oncorhynchus mykiss* population: synergy or one driving force
4.09P.24	**Josef Koch**	Antidepressant citalopram stimulates population growth of the harpacticoid copepod *Nitocra spinipes*
4.01P.6	**João Barbosa**	Mitochondrial toxicity of chemical mixtures: a tool for whole effluent testing
3.01P.4	**Qiyun Zhang**	Impact of use of the ionizable pH buffer MOPS on bioavailability research: tests with the cyanobacteria *Microcystis aeruginosa*
2.05P.6	**Simon Hansul**	Extrapolation of Metal Toxicity from Individuals to Communities in Three Daphnid Species: A DEB-based Approach

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